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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/693,754	10/20/2000	Neil Berinstein	13115	7885

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EXAMINER	
WEHBE, ANNE MARIE SABRINA	
ART UNIT	PAPER NUMBER
1633	
MAIL DATE	DELIVERY MODE
10/01/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/693,754	BERINSTEIN ET AL.	
	Examiner	Art Unit	
	Anne Marie S. Wehbe	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 May 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-19,21-27,32,33 and 35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 4-19, 21-27, 32-33, and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and response received on 5/17/00 has been entered. Claims 3, 20, 28-31, and 34 are canceled. Claims 1-2, 4-19, 21-27, 32-33, and 35 are pending in the instant application. An action on the merits follows.

Those sections of Title 35, US code, not included in the instant action can be found in the previous office action.

Claim Rejections - 35 USC 103

The rejection of previously pending claims 1-2, 4-17, and 32-35 under 35 U.S.C. 103(a) as being unpatentable over Hurpin et al. (1998) Vaccine, Vol. 16 (2/3) 208-215, in view of Hodge et al. (1997) Vaccine, Vol. 15, No. 6/7, 759-768, US Patent No. 6,127,116 (10/3/00), filed on 3/4/97 and hereafter referred to as Rice et al., and Lehner et al. (1999) J. Infect. Dis., Vol. 179 (Suppl 3), S489-S492, is maintained over claims 1-2, 4-17, 32-33, and 35, and withdrawn over canceled claim 34. Applicant's amendment and arguments have been fully considered but have not been found persuasive in overcoming the instant grounds of rejection for reasons of record as discussed in detail below.

The applicant argues that Hurpin et al. provides no reasonable expectation of success in generating an immune response using direct lymph node administration as claimed based on their success using intrasplenic delivery because the spleen and a lymph node are different types of lymphatic tissue. In response, this is not agreed as both the spleen and lymph nodes serve

similar functions in generating T and B cell mediated immune responses against lymph and blood contaminants such as bacteria, viruses, and other foreign matter, and are comprised of similar types of immune cells, including T and B cells, macrophages, and dendritic cells. Thus, it is maintained that based on the teachings of Hurpin et al., the skilled artisan would have expected that delivery of vaccine to a lymphatic tissue, whether spleen or lymph node, would generate an immune response and further that the immune responses generated would be increased over subcutaneous delivery.

The applicant provides no arguments concerning the teachings of Hodge et al. other than to say that Hodge et al. does not satisfy the deficiencies of Hurpin et al. Regarding Rice et al., the applicant reiterates their argument that Rice et al. does not cure the deficiencies of Hurpin et al. because Rice et al. does not provide sufficient support for an obviousness rejection, citing *PharmaStem Therapeutics Inc. v. Viacell Inc.* for the need for more than simply general guidance to establish obviousness. In response, the previous office action pointed out that Rice et al. specifically teaches that administration both directly and indirectly to a lymph node is the preferred method of immunization. Thus, Rice et al. provides clear direction to preferentially use direct intranodal administration to induce immune responses. As for *PharmaStem Therapeutics Inc. v. Viacell Inc.,* the portions previously cited by the applicant is actually a discussion of how *In re O'Farrell* provided guidance in the *PharmaStem* case. However, as discussed in previous rejections, the instant rejection is not one in which the prior art gave no direction as to which parameters were critical or as to which of many possible routes of choices would be likely to be successful, nor is the instant rejection one in which only general guidance was provided by the cited prior art. In the instant case, all of the cited references teach the importance of the route of

administration of antigen on generating immune responses. Further, Hurpin et al. specifically teaches administration to spleen, a lymphatic tissue, and Lehner et al. and Rice et al. specifically teach either the indirect or direct targeting of antigen to a lymph node.

The applicant then reiterates their argument that the technique used by Lehner et al. is similar to a subcutaneous injection technique and thus is very different from the claimed method of direct administration of the antigen to the lymph node. This is not agreed. As discussed in previous office actions, Lehner et al. was cited for demonstrating that the delivery of an antigen such that the lymph node is specifically targeted generates increased immune responses to the antigen as compared to other routes of administration. As stated in previous office actions, Lehner et al. showed that a direct comparison of intramuscular versus intradermal versus targeted iliac lymph node immunization revealed that targeted iliac lymph node administration of antigen resulted in increased T and B cell mediated antigen-specific immune responses (Lehner et al., page S489, and page S491). The targeted iliac lymph node administration technique, while subcutaneous, administers the antigen close to both the internal and external iliac lymph nodes, ensuring direct exposure of the lymph nodes to the administered antigen. As stated in the previous office action, the fact that the Lehner et al. publication cited in the instant rejection generated substantial antigen specific immune responses using their targeted iliac lymph node immunization technique whereas both Hurpin et al. and applicant were not able to generate antigen specific immune responses greater than controls using non-targeted subcutaneous administration provides clear evidence that targeted delivery of antigen in the vicinity of lymph node has a substantial effect in enhancing immune responses.

Finally, it is noted that the rejection of record is further based on the combined teachings of Hurpin et al., Hodge et al., Rice et al., and Lehner et al. and the knowledge available to the skilled artisan at the time of filing. Lehner et al., as discussed above and in previous office actions, clearly demonstrates successful generation of immune response by targeted administration of antigen in close proximity to lymph nodes. In addition, all of Hurpin et al., Rice et al., and Lehner et al., teach that lymphatic administration successfully generates immune responses, and Rice and Lehner et al. particularly point to targeting the lymph node either directly or indirectly with antigen to induce immune responses. Taken as a whole, the combined teachings of the cited references demonstrate that the skilled artisan at the time of filing would have had a reasonable expectation that direct intranodal administration of an antigen would induce an immune response. The applicant is also reminded that obviousness does not require absolute predictability of success; for obviousness under 35 U.S.C. § 103, all that is required is a reasonable expectation of success. See In re O'Farrell, 7 USPQ2d 1673 (CAFC 1988).

Therefore, applicant's arguments are not found persuasive and the rejection of record stands.

The rejection of claims 18-19 under 35 U.S.C. 103(a) as being unpatentable over Hurpin et al. (1998) Vaccine, Vol. 16 (2/3) 208-215, in view of Hodge et al. (1997) Vaccine, Vol. 15, No. 6/7, 759-768, US Patent No. 6,127,116 (10/3/00), filed on 3/4/97 and hereafter referred to as Rice et al., and Lehner et al. (1999) J. Infect. Dis., Vol. 179 (Suppl 3), S489-S492, as applied to claims 1-2, 4-17, 32-33, and 35 above, and further in view of Zaremba et al. (1997) Canc. Res., Vol. 57, 4570-4577 and Salgaller et al. (1996) Canc. Res., Vol. 56, 4749-4757, is maintained.

Applicant's arguments have been fully considered but have not been found persuasive in overcoming the instant grounds of rejection for reasons of record as discussed in detail below.

Applicant's arguments are based on their previous argument that Hurpin in view of Hodge, Rice, and Lehner do not support a *prima facie* case of obviousness. These arguments have been fully considered and addressed in detail above and have not been found persuasive. Applicant's further argument that Zaremba et al. and Salgaller et al. do not overcome the deficiencies of Hurpin, Hodge, Rice, and Lehner is not persuasive as the teachings of Hurpin, Hodge, Rice, and Lehner stand, as discussed above, and Zaremba and Salgaller were not cited to teach lymph node administration, rather these references were cited to provide teachings and motivation to immunize with tumor antigens which comprise the sequence YLSGADLNL or YLEPGPVTV. The applicant has not traversed these teachings, therefore, the rejection of record stands.

The rejection of claims 21-27 under 35 U.S.C. 103(a) as being unpatentable over Hurpin et al. (1998) Vaccine, Vol. 16 (2/3) 208-215, in view of Hodge et al. (1997) Vaccine, Vol. 15, No. 6/7, 759-768, US Patent No. 6,127,116 (10/3/00), filed on 3/4/97 and hereafter referred to as Rice et al., and Lehner et al. (1999) J. Infect. Dis., Vol. 179 (Suppl 3), S489-S492, as applied to claims 1-2, 4-17, 32-33, and 35 above, and further in view of Barnett et al. (1997) Vaccine, Vol. 15(8), 869-873, is maintained. Applicant's arguments have been fully considered but have not been found persuasive in overcoming the instant grounds of rejection for reasons of record as discussed in detail below.

Applicant's arguments are based on their previous argument that Hurpin in view of Hodge, Rice, and Lehner do not a *prima facie* case of obviousness These arguments have been fully considered and addressed in detail above and have not been found persuasive. Applicant's further argument that Barnett does not overcome the deficiencies of Hurpin, Hodge, Rice, and Lehner is not persuasive as the teachings of Hurpin, Hodge, Rice, and Lehner stand, and Barnett was not cited to teach lymph node administration. Rather, Barnett was cited to provide teachings and motivation to immunize using a prime/boost vaccination strategy which includes a priming step with a nucleic acid encoding an antigen and a boosting step with a protein form of the antigen. The applicant has not traversed these teachings, therefore, the rejection of record stands.

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Joseph Woitach, can be reached at (571) 272-0739. For all official communications, the technology center fax number is (571) 273-8300. Please note that all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197. Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

/Anne Marie S. Wehbé/
Primary Examiner, A.U. 1633